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Lung volume and its correlation to nocturnal apnoea and desaturation

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The cross-sectional area of the upper airway is known to be lung volume dependent. If, and to what extent, lung volume variables correlate to nocturnal obstructive apnoeas and oxygen desaturations independently of other factors known to affect lung volumes and sleep disordered breathing is still unclear.

A total of 92 subjects were examined by ambulatory recording of nocturnal obstructive apnoeas and desaturations. Sixty-nine of the subjects had a history of snoring and 23 were healthy subjects without complaints of snoring and daytime sleepiness. All subjects performed static and dynamic spirometry for measurements of lung volumes. To evaluate the correlation between lung volume variables and apnoea index (AI) and oxygen desaturation index (ODI), simple and multiple regression analysis was performed.

Expiratory reserve volume (ERV) was found to be lower in subjects with snoring and apnoeas (ERV = 1·0 l) than in non-snoring subjects (ERV = 1·7 l), ($P < 0{\cdot}001$). Forced expiratory volume in 1 sec (FEV_1)/vital capacity (VC) was slightly, but significantly ($P = 0{\cdot}031$), lower in subjects with snoring and nocturnal apnoeas and desaturations. In the multiple regression analysis ERV was found to be independently correlated to both AI ($R^2 = 0{\cdot}13$; $P = 0{\cdot}001$) and ODI ($R^2 = 0{\cdot}11$; $P = 0{\cdot}002$). Multiple regression analysis also revealed that ERV, body mass index (BMI) and habitual smoking together accounted for 43% of the variation in AI and 48% of the variation in ODI.

We find a significant independent association between ERV and nocturnal obstructive apnoea and oxygen desaturation frequency. Our results indicate that ERV is correlated to these events to a similar extent, as is obesity.

Key words: snoring; obstructive sleep apnoea; lung volumes; sleep disordered breathing.

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Introduction

Today snoring and obstructive sleep apnoea (OSA) is recognized as a relatively common disease among men and women (1,2). In spite of the attention that has been paid to the disease in recent decades, there is still a great deal of uncertainty about the pathophysiological mechanisms that cause the upper airway to collapse.

It has been shown that the cross-sectional area of the pharynx is lung volume dependent (3,4) and previous studies have also implicated an association between a reduced or low lung volume and nocturnal obstructive apnoeas and desaturations (5,6,7,8). However, obesity is a common feature in patients with OSA (9) and obesity is also known to alter lung function, preferably by a reduction in expiratory reserve volume (ERV) and functional residual capacity (FRC) (10,11). If, and to what extent, lung volume variables correlate to nocturnal obstructive apnoeas and oxygen desaturations independently of other factors known to affect lung volumes and sleep disordered breathing is still unclear.

The aim of the present study was to evaluate the association between lung volume variables, measured during wakefulness, and nocturnal obstructive apnoea and desaturation frequency.

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Population and methods

POPULATION

The study population consisted of the same 103 subjects as described in a previous publication (12). Subjects with a history of asthma or other lung disease ($n = 11$) were excluded from the present investigation. The remaining population consisted of 69 subjects referred to the clinic for an investigation of snoring and of 23 healthy non-snoring

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control subjects. The subjects were 68 men, aged 27–70 years (mean 47), and 24 women, aged 37–67 years (mean 53).

The non-snoring subjects were randomly selected from the local municipality population register. Initially, a total of 400 subjects were asked by letter if they had any problems with snoring and/or daytime sleepiness and if they would be positive to participate in the study. Answers were received from 346 subjects (86·5%). Eighty-four subjects (21%) denied problems of snoring and daytime sleepiness and were also willing to take part in the investigation. From this group 33 randomly selected subjects underwent a nocturnal apnoea and saturation screening investigation. Twenty-three subjects were without a history of lung disease and had an AI and ODI of less than 5 and were finally included into the study. The study protocol was examined and approved on by the local ethics committee.

ANTHROPOMETRY AND NIGHT RECORDING

The height and weight of all subjects was measured. With regard to the history of smoking the subjects were classified as never smoked, ex-smokers (stopped smoking a year or more ago) and habitual smokers.

As described previously (12), the subjects underwent a nocturnal registration of apnoeas and desaturations during one night in their homes, using a validated unattended recording device, MicroDigitrapper-S (M-S), Synectics Medical, Stockholm, Sweden (13). The following registered parameters were analysed to detect nocturnal obstructive breathing and obstructive apnoeas: oronasal flow (thermistor), chest movement (mattress — with a polyvinylden-fluoride motion sensor), abdominal respiration movement (piezoelectric belt positioned at the level of the diaphragm). Arterial oxygen saturation was measured by a finger pulse oximeter. Analysis of the recordings was performed using an analysis program — Multigram SA (TM, Synectics Soft., Stockholm, Sweden & Dallas, U.S.A.) software package. Each recording was examined visually by one person and apnoeas and oxygen desaturations were rated manually. By definition, an apnoea was scored when airflow ceased in the nose and mouth for at least 10 sec (14) and a desaturation was defined as a drop in saturation level of 4% or more from the previous baseline (15). A desaturation that occurred without a preceding apnoea was interpreted as being caused by a hypopnoea rather than being a false positive desaturation (15). Both the apnoea index (AI = number of apnoeas h^{-1}) and oxygen desaturation index (ODI = number of 4% desaturations h^{-1}) were calculated on the basis of total time in bed.

SPIROMETRY

Static and dynamic spirometry was performed using a body plethysmograph (SensorMedics Autobox D_L 6200). Vital capacity (VC), forced vital capacity in 1 sec (FEV_1), functional residual capacity (FRC) and airway resistance (RAW) were measured. Expiratory reserve volume (ERV), residual capacity (RV) and total lung capacity (TLC) were calculated. Measurements and calculations of lung volumes were performed in accordance to standard criteria's (16,17).

STATISTICAL ANALYSIS

When group comparisons were performed, the Mann–Whitney *U*-test was used. Correlation coefficients were computed using Spearman's rank correlation coefficient.

Multiple regression analysis was performed with AI and ODI as dependent variables. Since the distributions of both AI and ODI were positively skewed, log transformation of these variables was performed before the analysis. Moreover, some of the dependent variables were transformed to make a linear model applicable. We also performed an analysis to find factors correlating to the lowest saturation value measured during the nocturnal registration ($SaO_2\%_{min}$). In this analysis, the $SaO_2\%_{min}$ was set as the dependent value and factors known to influence this variable were used as explanatory variables.

Stepwise regression analysis was used as the variable selection strategy. The set of dependent variables were: age, sex, smoking factor, BMI, weight, height, FEV_1, FEV_1/VC, VC, TLC, RV, RV/TLC, FRC, ERV and RAW. The smoking factor was defined as: 0 = never smoked and ex-smoker; 1 = habitual smoker. Regression diagnostics was performed by analysing residuals and the influence of outliers. In all analyses, a *P*-value equal to or less than 0·05 was considered statistically significant.

Results

Nocturnal apnoea and desaturation registration showed that among subjects with a history of snoring 23 subjects had an AI and ODI of <5, 15 subjects had an AI <5 and an ODI of ≥ 5 and finally 31 subjects had both AI and ODI of ≥ 5.

COMPARISON OF DATA

Overall data for the subjects are displayed in Table 1. As expected, patients with a history of snoring were more obese than subjects in the non-snoring group. Expiratory reserve volume (ERV) as well as the FEV_1/VC value was significantly lower ($P < 0{\cdot}001$ and $P = 0{\cdot}031$ respectively) in the group with snorers and OSA patients.

CORRELATION ANALYSIS

Both weight and BMI were significantly correlated to AI and ODI (Table 2). Among the lung volume variables received from the spirometry, ERV, FRC, FEV_1/VC and RAW were all found to be significantly correlated to AI while a significant correlation to ODI were found for ERV and FRC (Table 2). Regarding lung volumes, FRC, ERV and RAW values were significantly correlated to $SaO_2\%_{min}$.

TABLE 1. Night recording, anthropometric and spirometric data

	Non-snorers ($n=23$)		Snorers ($n=69$)		
	Mean (SD)	Range	Mean (SD)	Range	*P*-value*
Anthropometric data					
Sex (M/F)	14/9	—	51/15	—	—
Smoke (N/E/H)	13/6/3	—	21/21/25	—	—
Age (y)	49·7 (10·8)	32–68	48·2 (9·2)	27–70	n.s.
Height (cm)	174·6 (7·7)	164–194	175·1 (8·5)	154–190	n.s.
Weight (kg)	77·7 (12·5)	59–124	91·0 (18·0)	64·5–150	<0·001
BMI (kg m^{-2})	25·8 (3·7)	20·0–36·7	29·8 (6·5)	21·2–58·6	0·002
Night recording data					
Total time in bed (h)	7·0 (2·0)	1·1–12·3	6·8 (1·4)	4·2–12·4	n.s.
AI (apnoeas h^{-1})	0·3 (0·8)	0–3	15·7 (23·4)	0–111	<0·001
ODI (desaturations h^{-1})	1·4 (1·2)	0–3	25·2 (27·6)	0–106	<0·001
Max. apnoea length (sec)	8·6 (13·0)	0–47	33·6 (25·5)	0–114	<0·001
$SaO_2\%_{min}$ (%)	88·4 (2·8)	84–93	78·8 (10·5)	50–94	<0·001
Spirometric data					
FEV_1 (l)	3·6 (0·8)	2·3–5·1	3·5 (0·8)	1·9–5·4	n.s.
VC (l)	4·5 (0·9)	3·2–6·3	4·6 (1·0)	2·6–6·7	n.s.
FEV_1/VC	79·2 (6·3)	63·9–89·4	75·1 (7·4)	55·2–86·1	0·031
FRC (l)	3·1 (1·1)	1·1–4·8	3·1 (0·8)	1·3–5·2	n.s.
ERV (l)	1·7 (0·6)	0·5–2·9	1·0 (0·6)	0·04–2·7	<0·001
RV (l)	1·8 (0·4)	1·2–2·7	2·1 (0·6)	0·8–3·2	n.s.
TLC (l)	6·6 (1·3)	4·6–9·0	6·7 (1·2)	3·8 (9·3)	n.s.
RV/TLC	30·9 (8·1)	18·7–59·3	31·3 (6·4)	19·4–45·9	n.s.
RAW (kPa^{-1} sec^{-1})	0·141 (0·076)	0·05–0·370	0·145 (0·067)	0·01–0·400	n.s.

AI: apnoea index; ODI: oxygen desaturation index; N: never smoked; E: ex-smoker; H: habitual smoker; BMI: body mass index; VC: vital capacity; FEV_1: forced expiratory volume in 1 sec; FRC: functional residual capacity; ERV: expiratory reserve volume; RV: residual volume; TLC: total lung capacity; RAW: airway resistance; Values represent the mean value and the standard deviation (SD). *Mann–Whitney *U*-test.

TABLE 2. Univariate relationship between apnoea index (AI), nocturnal oxygen desaturation index (ODI), $SaO_2\%_{min}$ and anthropometric and spirometric variables [values represent the correlation coefficient, *r* and the *P*-value (*P*)]

	AI		ODI		$SaO_2\%_{min}$	
Age	0·13	(n.s.)	0·05	(n.s.)	−0·15	(n.s.)
Height (cm)	−0·07	(n.s.)	−0·09	(n.s.)	0·19	(n.s.)
Weight (kg)	0·53	(<0·001)	0·58	(<0·001)	−0·51	(<0·001)
BMI (kg m^{-2})	0·52	(<0·001)	0·63	(<0·001)	−0·60	(<0·001)
FEV_1 (l)	−0·10	(n.s.)	−0·11	(n.s.)	0·20	(n.s.)
VC (l)	−0·06	(n.s.)	−0·09	(n.s.)	0·19	(n.s.)
FEV_1/VC	−0·24	(0·025)	−0·15	(n.s.)	0·20	(n.s.)
FRC (l)	−0·23	(0·030)	−0·35	(0·001)	0·39	(<0·001)
ERV (l)	−0·55	(<0·001)	−0·55	(0·001)	0·60	(<0·001)
RV (l)	0·13	(n.s.)	0·14	(n.s.)	−0·11	(n.s.)
TLC (l)	−0·02	(n.s.)	−0·10	(n.s.)	0·17	(n.s.)
RV/TLC	0·14	(n.s.)	0·30	(n.s.)	0·06	(n.s.)
RAW (kPa^{-1} sec^{-1})	0·22	(0·046)	0·19	(n.s.)	0·26	(0·016)

For a definition of abbreviations, see Table 1.

MULTIPLE REGRESSION ANALYSIS

In the multiple regression analysis, ERV remained as an independent significant predictor of AI and ODI (Table 3). When it came to obesity variables, BMI also remained as an independent predictor of these dependent variables as was habitual smoking. Analysis revealed that these three variables together accounted for 43% of the variation in AI and 48% of the variation in ODI. We included weight instead of BMI in the equation and found that the partial correlation coefficient between ERV and AI increased somewhat ($R^2 = 0{\cdot}22$; $P < 0{\cdot}001$), as did the partial correlation coefficient for ERV and ODI ($R^2 = 0{\cdot}22$; $P < 0{\cdot}001$). In the multiple regression analysis with $SaO_2\%_{min}$ as the dependent value, as much as 75% of the variation was explained by four independent variables, maximum apnoea length ($R^2 = 0{\cdot}49$; $P < 0{\cdot}001$), BMI ($R^2 = 0{\cdot}19$; $P = 0{\cdot}001$), ERV ($R^2 = 0{\cdot}06$; $P = 0{\cdot}032$) and TLC ($R^2 = 0{\cdot}035$; $P = 0{\cdot}035$).

Using the equations from the regression models (AI = Exp[−7·116 − 1·468*Sqrt[ERV] + 2·732*Log[BMI] + 0·576*Habitual smoking] and ODI = Exp[−9·209 − 1.285 *Sqrt[ERV]+3·501*Log[BMI]+0·576*Habitual smoking]), we exemplify the effect of the different predictors on AI and ODI in Figs 1 and 2. The figures graphically display the independent correlation between ERV and AI and ODI. For two persons with the same BMI and the same smoking status (habitual smoker or never smoked/ex-smoker), the model shows that the expected number of apnoeas and desaturations is higher for a person with a low ERV. It can also be seen that a decrease in ERV of 1 l at a normal ERV level results in a lower increase in AI and ODI than a decrease in ERV at an already low level.

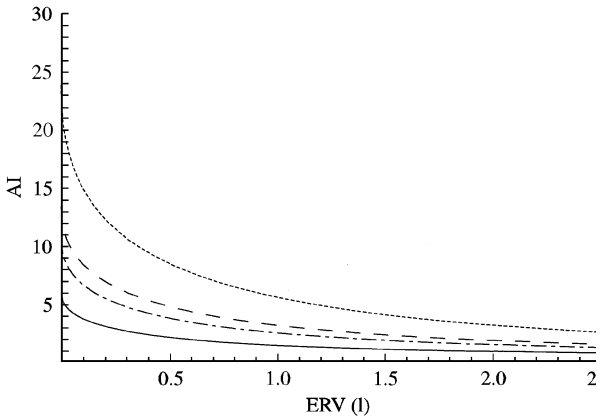

FIG. 1. The diagram shows the influence of expiratory reserve volume (ERV, l) on the apnoea index (AI) in a non-obese (BMI = 26) non-smoking subject (continuous line), a non-obese (BMI = 26) smoking subject (dotted-dashed line), an obese (BMI = 35) non-smoking subject (dashed line) and an obese (BMI = 35) smoking subject (dotted line).

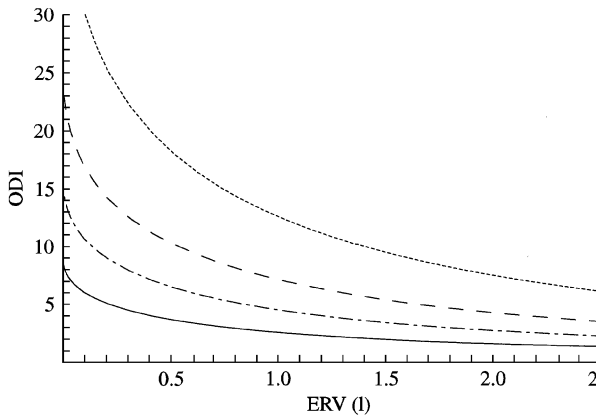

FIG. 2. The diagram shows the influence of expiratory reserve volume (ERV, l) on the oxygen desaturation index (ODI) in a non-obese (BMI = 26) non-smoking subject (continuous line), a non-obese (BMI = 26) smoking subject (dotted-dashed line), an obese (BMI = 35) non-smoking subject (dashed line) and an obese (BMI = 35) smoking subject (dotted line).

Discussion

The present study, carried out on a large number of subjects with and without snoring and data compatible with obstructive sleep apnoea, presents results of a significant association between expiratory reserve volume (ERV) and the frequency of nocturnal obstructive apnoeas (AI) and oxygen desaturations (ODI). We have also shown that this association is present after adjusting for other factors known to affect sleep disordered breathing, such as obesity and habitual smoking, as well as factors known to affect lung volume itself. ERV was also found to correlate independently, although to a lesser extent, to the lowest nocturnal $SaO_2\%_{min}$. These results are interesting since they indicate that the predictive value of a low ERV is similar to that of obesity in predicting nocturnal apnoeas and desaturations.

TABLE 3. Variables which were independently related to the apnoea index (AI) and oxygen desaturation index (ODI)

	AI $R^2 = 0{\cdot}43$	ODI $R^2 = 0{\cdot}48$
ERV (l)	$R^2 = 0{\cdot}13$ $P = 0{\cdot}001$	$R^2 = 0{\cdot}11$ $P = 0{\cdot}002$
BMI (kg m^{-2})	$R^2 = 0{\cdot}10$ $P = 0{\cdot}003$	$R^2 = 0{\cdot}17$ $P < 0{\cdot}001$
Habitual smoking	$R^2 = 0{\cdot}06$ $P = 0{\cdot}028$	$R^2 = 0{\cdot}06$ $P = 0{\cdot}021$

For a definition of abbreviations, see Table 1.

Previous reports have suggested that the cross-sectional area of the upper airway is lung volume dependent, a phenomenon most pronounced in patients with OSA (3,4) and at low lung volume. The change in cross-sectional area following a decrease in lung volume has also been reported to independently correlate to the apnoea/hypopnoea index (AHI) (18). Önal *et al*. (5) reported that functional residual capacity (FRC) and inspiratory airway conductance (GAW) were correlated to AHI in a group of 34 patients with OSA. In our study, RAW displayed a significant correlation to AI but did not remain as an independent predictor in the multivariate analysis. This could be explained by the fact that RAW has been shown to increase when lung volume decreases (19).

The physiological mechanisms explaining the correlation between low lung volume and upper airway closure during sleep are not fully understood. It is, however, probable that different reflex mechanisms are involved. When lung volume decreases, a more negative inspiratory pressure is seen (20). Normally, the activity of both the laryngeal muscles and the diaphragm increase when negative inspiratory pressure increases (21). However, the activity of the genioglossus muscle is insufficient to compensate for negative pressure at the onset of upper airway occlusion in obese patients with OSA, 'the balance of pressures concept' (22). In addition, subjects with OSA have an impaired capability to increase respiratory muscle drive during increased mass loading compared with equally obese subjects without OSA (23).

Our results, which indicate that ERV and not FRC is independently correlated to ODI and the lowest nocturnal SaO_2%, are in agreement with the results presented by Sériès *et al*. (6). They reported that the fall in SaO_2% in subjects with OSA is highly correlated to lung volume, a phenomenon also seen in the healthy subject (24). The hypothesis of low lung volume as a determinant of nocturnal hypoxemia in subjects with OSA is also supported in a report by Bradley *et al*. (8), which shows that expiratory reserve volume is strongly correlated to nocturnal mean SaO_2%. The physiological mechanism may be that there is an increase in the closure of peripheral airways, especially in the lower dependent regions of the lung (25). Our results also show that the length of the apnoea is a determining factor for the lowest nocturnal SaO_2%.

We found obesity to be an independent predictor of both AI and ODI, a correlation that is well known (26,27,28,29). In addition, smoking has been suggested as a risk factor for OSA (30), possibly since smoke could cause oedema and inflammation in the tissue in the upper airway and thus have a negative effect on cross-sectional area (31). In our study, a weak but significant correlation between habitual smoking and AI and ODI was found.

We chose to study actual lung volume variables and not the variables expressed as a percentage of a predicted normal value. Obesity is known to affect lung volume (10,11) and the possibility of lung volume related co-founders influencing our results was therefore taken into account in the multiple regression analysis where adjustments were made for both weight and BMI. In addition, other factors known to influence lung volume such as age, height, smoking and sex were also taken into account in the multiple regression analysis.

Chronic obstructive pulmonary disease has been shown to co-exist in some patients with OSA (32,33). It has also been suggested that asthma may be associated with increased daytime sleepiness (34), the latter also being a symptom of OSA. In order to reduce the possibility of bias due to these factors, no subject with a history of any lung disease was included in the study. In addition we made adjustments for variables known to describe airway obstruction such as FEV_1, FEV_1/VC, RV/TLC and RAW in the multiple regression analysis. In our group of subjects, FEV_1/VC and RAW were correlated to AI, but these variables did not remain as independent predictors in the multivariate analyses. Smoking is well known to affect the lungs and the airways and thus also lung function variables such as FEV_1 and VC. Thus the difference in FEV_1/VC found between non-snorers and snorers could be secondary due to the differences in the ratio of habitual smokers/non-smoker between the two groups. The smoking factor could also be one possible cause as to why we did not find an independent association between airway obstruction and AI/ODI. Others (34,35,36) have described a correlation between airway obstruction and sleep apnoea severity.

However, the fact that ERV and not FRC were independently correlated to AI/ODI may reflect the presence of diffuse airway obstruction. As mentioned earlier, Bradley *et al*. (8) found that ERV was an independent predictor of nocturnal mean SaO_2% while FRC was not. In that report it was discussed and concluded that this could be due to a combination of obesity and diffuse airway obstruction. ERV may be affected in two ways. First obesity may effect ERV by decreasing FRC. Secondly, ERV may be decreased by an increase in residual volume (RV) caused by increase in airway closure. Especially in obesity the reduction in ERV may be associated with closure of small peripheral airways (37).

A limitation with the present study is that sleep was not registered and this should be kept in mind when interpreting the significance of our results. Thus, both AI and ODI may have been underestimated since calculations of indices were made on total time in bed and not on total sleep time. Since lung volume is reduced both by supine position and by sleep it should also be stated that in the present study, lung volume was measured during wakefulness and in the sitting position.

In conclusion, we find a significant correlation between ERV and both nocturnal apnoea and desaturation frequency. This correlation is still present after adjusting for confounding factors such as obesity and smoking. Our results indicate that ERV is associated with nocturnal apnoeas and desaturations to a similar extent, as is obesity. Our results could indicate that increased airway resistance contributes to nocturnal apnoea and desaturation frequency.

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